Specialty Conference

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Non-Invasive Methods for the Assessment of Cardiac Function

DR. JOHN ROSS, JR.:* Since Cournand and Richard's implementation of precise methods for hemodynamic study of the right side of the heart, direct cardiac catheterization has remained the standard tool for the assessment of circulatory dynamics. The subsequent development of methods for entering the left side of the heart and for selective angiocardiography, together with further improvements in instrumentation, have added to the usefulness and further improved the precision of such techniques. Nevertheless, these invasive procedures carry the risk of catheter-induced vascular and cardiac complications, and the search for suitable non-invasive methods for examination of the heart and circulation has been a continuing one. There remains a clearcut need for techniques that will permit study of cardiac patients in serial fashion, and during various forms of stress, reliably and without hazard.

The present conference will focus on several types of non-invasive studies that have seen substantial advances in the past few years. In examining the usefulness of each of these approaches it is desirable, of course, to test their validity against the standardized invasive methods of cardiac catheterization and angiography, and each of the investigators participating in this conference has directed some attention toward this goal. The non-invasive techniques that we shall examine today include external recording of the pulse waves and heart sounds (the so-called systolic time intervals); plain radiographic and video techniques for examining heart size and motion; the use of ultrasound for obtaining dynamic anatomic information about the heart and great vessels; and the use of radioisotopes.

The recording of an indirect carotid pulse wave tracing, together with the electrocardiogram and a recording of the heart sounds, constitutes one of the earliest methods used for estimating the

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functional state of the left ventricle. Several recent studies have shown good statistical correlations between the angiographic methods for evaluating left ventricular function and the systolic time intervals. Dr. Robert O'Rourke will open the discussion by reviewing the current status of these methods and some of the factors that influence their reliability.

DR. ROBERT O'ROURKE:* The indirect measurement of the pre-ejection period (PEP) and the left ventricular ejection time (LVET), often termed the systolic time intervals (STI), has found increasing use in patients with a variety of cardiac disorders. Studies in several laboratories suggest that measurement of the STI may provide a non-invasive yet sensitive means for detecting depression of left ventricular function, particularly when applied serially in the individual patient.[1-5] In addition, the STI clearly can distinguish groups of patients with left ventricular failure from normal subjects; however, they appear less reliable for separating patients with compensated heart disease from normal subjects, either under resting conditions or during exercise.[6] Moreover, the STI can be influenced by a number of hemodynamic variables, several of which may be operative simultaneously in a given subject. Therefore, considerable controversy remains as to the accuracy with which the STI reflect left ventricular function in the individual cardiac patient.[6,7]

The measurement of left ventricular STI requires the simultaneous recording of a high frequency phonocardiogram, the indirect carotid arterial pulse waveform, and the electrocardiogram on a multichannel recorder at a paper speed of at least 100 mm per second. The recordings are made with the subject supine and in the basal, post-absorptive state.[1,3] Calculations of the mean systolic time intervals are based upon the measurement of at least ten cardiac cycles, beginning and ending with the same phase of respiration.

Electromechanical systole ($Q\text{-}S_2$ interval) encompasses the period from the onset of the QRS complex to the first high frequency deflection of the aortic component of the second heart sound (Figure 1). The left ventricular ejection time (LVET) begins with the upstroke of the carotid arterial pulse and ends with the dicrotic notch (Figure 1). This interval correlates closely with the same interval measured from the intra-aortic

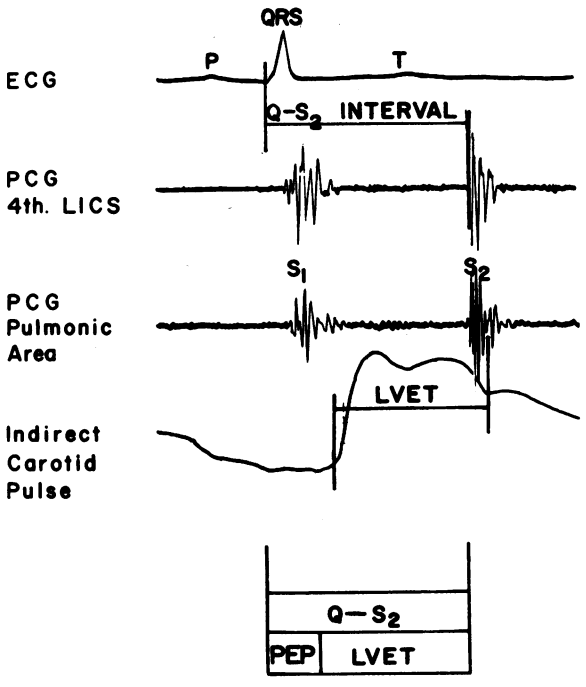

Figure 1.—Systolic time intervals in a normal subject. ECG is the electrocardiogram; PCG, the phonocardiogram; LVET is the left ventricular ejection time; PEP is the pre-ejection period; and $Q\text{-}S_2$ is electromechanical systole. LICS is left intercostal space. (From Johnson AD, O'Rourke RA, Karliner JS, and Burian C: Effect of myocardial revascularization on systolic time intervals in patients with left ventricular dysfunction. Circulation 45 (Suppl 1):91, 1972. Reproduced by permission of the American Heart Association, Inc.)

pressure pulse tracing. The pre-ejection period (PEP) is the difference between the duration of left ventricular electromechanical systole and the LVET, that is, $PEP = (Q\text{-}S_2)\text{-}LVET$. The PEP can be further divided into the Q to S_1 interval and the period of isovolumetric contraction (ICT).

Factors which influence the LVET include the heart rate, stroke volume, left ventricular afterload, the myocardial inotropic state, and the sex of the patient (Figure 2).[1,2] Unfortunately, in the individual patient there may be changes in several of these variables simultaneously, each change having a different effect on the left ventricular ejection time. For example, the administration of a positive inotropic agent such as digitalis to a patient with left ventricular failure and a diminished stroke volume would have two opposite effects on the LVET. The increase in stroke volume resulting from the increase in myocardial contractility would tend to increase the LVET while the increase in the velocity of ventricular ejection would tend to shorten it.

Factors which influence the PEP include heart

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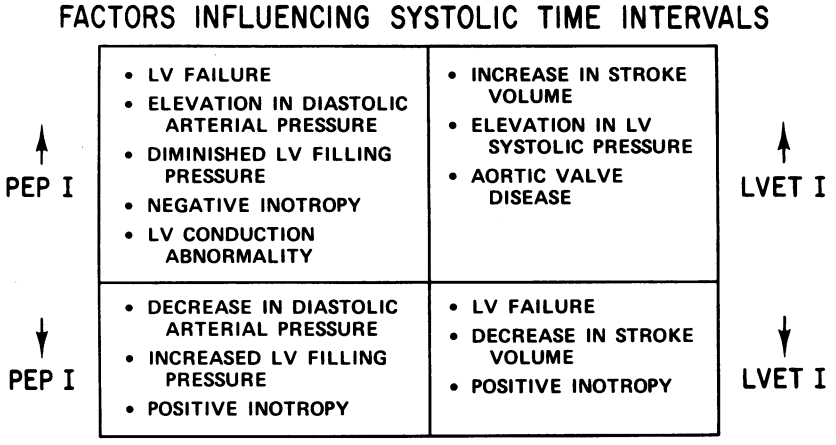

Figure 2.—Schematic representation of the effects of various hemodynamic alterations on the pre-ejection period index (PEP I) and the left ventricular ejection time index (LVET I).

rate, aortic diastolic pressure, the duration of the QRS complex, left ventricular filling pressure, and the inotropic state of the myocardium (Figure 2).[1,2] Accordingly, in patients with cardiogenic shock, a high left ventricular end-diastolic pressure and a low aortic diastolic pressure may result in a short PEP despite depressed left ventricular function. On the other hand, a normally or mildly elevated left ventricular end-diastolic pressure and a normal aortic diastolic pressure usually is accompanied by appreciable prolongation of the PEP when myocardial contractility is depressed, because of the reduced rate of isovolumic pressure development (dP/dt).

Systolic time intervals can be corrected for both heart rate and the patient's sex by using regression equations derived from data obtained in a large number of resting subjects without evidence of heart disease. Currently, there are no equivalent data on the relationship of STI to heart rate in normal subjects during supine and upright exercise. In the resting subject, the ratio of the PEP to the LVET (PEP:LVET) varies within narrow limits and need not be corrected for heart rate or sex. Deviations of PEP, LVET and QS_2 from normal may be represented by the difference between the observed measurements, uncorrected for heart rate and sex, and those predicated for the patient's heart rate and sex from the appropriate regression equation.[1,2] Another method of evaluating these measurements is to correct the observed values for heart rate and sex (systolic time interval indices) and compare the results to the normal range of corrected values.[1,2] The STI indices are calculated as the sum of the measured intervals and the product of the observed heart rate and the appropriate normal regression slope. For example, the LVET index in male subjects = 1.7 heart rate (HR) + the measured LVET (Table 1).

During left ventricular failure the PEP lengthens, the LVET diminishes, and the duration of electromechanical systole remains unchanged. These altered relationships may be expressed as an increase in the PEP:LVET ratio during left ventricular failure. The normal ratio in the basal state is 0.345 ±0.036 (1SD).[3] Several studies have shown a significant inverse correlation between the PEP:LVET ratio and the ejection fraction (stroke volume/end-diastolic volume) obtained by left ventricular cineangiography in patients with a variety of cardiac diseases.[3,5] In the presence of left ventricular failure, the increased pre-ejection period reflects the diminished rate of myocardial tension development, and the diminished left ventricular ejection time reflects the decreased stroke volume and reduced rate of myocardial fiber shortening.

Recently, we compared STI with measurements of the left ventricular ejection fraction (stroke

TABLE 1.—*Systolic Time Indices in Normal Subjects**

Measurement	*Equation*	*Normal Range*
$Q\text{-}S_2$ index (male)	$Q\text{-}S_2$ interval + 2.1 HR	530 - 560 msec
$Q\text{-}S_2$ index (female)	$Q\text{-}S_2$ interval + 2.0 HR	same
LVET index (male)	LVET interval + 1.7 HR	408 - 428 msec
LVET index (female)	LVET interval + 1.6 HR	same
PEP index (male)	PEP interval + 0.4 HR	118 - 144 msec
PEP index (female)	PEP interval + 0.4 HR	same

*HR is the heart rate and msec is milleseconds.

volume/end-diastolic volume) and the mean velocity of circumferential fiber shortening (mean Vcf) as measured from biplane left ventricular cineangiograms in patients with coronary artery disease or primary myocardial disease.[8,9] The direct and indirect studies were made on the same day in each patient. The results showed a good inverse correlation between the PEP:LVET ratio and the left ventricular ejection fraction (LVEF) ($r = -0.77$, $p < .001$) and the mean rate of circumferential fiber shortening (mean Vcf) ($r = -0.60$, $p < .001$). The correlation between PEP:LVET and either LVEF or mean Vcf was similar in patients with or without abnormal left ventricular wall motion. In this study, as in others, the measurement of STI clearly separated a group of normal patients from a group of patients with moderate or severe depression of left ventricular function. However, discordant results between STI and cineangiographic measurements of left ventricular function often occurred in individual patients within both groups. STI measurements suggested depressed left ventricular function in several patients with normal LVEF and mean Vcf, and were normal in other patients with cineangiographic evidence of reduced left ventricular function. This finding is not surprising considering the number of variables that can influence the measured STI, and the large standard deviation for the normal ratio of PEP:LVET.

We have found the serial measurement of STI to be useful in following individual patients with coronary artery disease and for evaluating the effect of interventions (vein bypass graft operation, propranolol therapy) on left ventricular function.[10,11] However, in several instances we have observed changes in STI which were not substantiated by a repeat left ventricular cineangiographic study, and occasionally *no* alterations occurred in STI despite pronounced reduction in left ventricular function on repeat cardiac catheterization after operation.

We may conclude that measurement of STI provides a useful means for the non-invasive evaluation of left ventricular function, particularly for separating groups of normal patients from patients with moderate to severe depression of left ventricular function. However, the available data suggest that the STI cannot always separate the individual patient with cardiac disease and mild to moderate left ventricular dysfunction from the subject with normal cardiac function. The major problem in interpreting STI, even in the same patient during periods of follow-up, is the difficulty in accounting for all of the hemodynamic variables that may be operative at the time of a given measurement. Nevertheless, serial recordings of the STI provide a non-invasive means for patient follow-up that often can alert the physician to the presence of depressed left ventricular function, and also add confidence to a clinical diagnosis of normal cardiac function.

Dr. Ross: Perhaps the first non-invasive means for examination of the heart, if we used the term non-invasive to indicate lack of intravascular catheter insertions, was the diagnostic chest x-ray film, and subsequently electrokymography also found considerable application. At the conference on myocardial infarction two years ago[12] we reviewed the use of standardized plane roentgenographic techniques for assessing left ventricular size, as well as radarkymography, a technique which employs a radar tracking circuit during image intensification fluoroscopy for obtaining an analog signal of cardiac wall motion. Drs. Kirk Peterson and Philip Ludbrook now have had considerable experience with an improved device for assessing wall motion abnormalities by use of a video-radiographic method and will describe the current status of this approach.

DR. KIRK PETERSON* AND DR. PHILIP LUDBROOK:† The analysis of left ventricular wall motion is of significant importance in the evaluation of the hemodynamics and mechanics of contraction in various cardiac disease states. Left ventricular cineangiography has provided the most direct and accurate means of recording wall motion in man,[13] but it is limited by its dependence on cardiac catheterization, lack of applicability to acutely ill patients, and unsuitability for serial observations. Non-invasive radiographic methods, including roentgenkymography and electrokymography,[14-16] have been used in the past but their successful application was hampered by lack of resolution, alinearity, poor frequency response or impracticability of operation. Apexcardiography and kinetocardiography[17,18] likewise are limited because the area of left ventricle examined is small and because of signal degradation imposed by the intervention of the chest wall between the heart and the recording transducer.

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The recent development of video-tracking devices now provides a reliable and relatively sensitive method for assessing left ventricular wall motion without the need for intracardiac instruments or catheters.[19,20] Such devices have proved useful for detecting the presence or absence of areas of segmental wall motion disorder, for assessment of serial changes in hypokinesis or dyskinesis during the course of an acute myocardial infarction, and for elucidation of the effects of pharmacologic agents on regional myocardial contraction.[21-23] They have future potential for non-invasive detection of abnormal diastolic filling patterns, quantitation of left ventricular compliance or distensibility and assessment of extent and velocity of myocardial shortening. In initial clinical studies, the Radarkymograph (RKY)* was used.[19] More recently, an improved Video Dimension Analyzer (VIDIAN)† with superior frequency response and ease of operation has been employed for microvascular studies in animals[20] and is now used in our laboratory for the study of cardiac pathophysiology in man.[21]

The black-white interface of the border of the heart and lung recorded during fluoroscopy is transmitted to the television circuit along each raster line as a change in voltage. When differentiated, this signal can be captured by the tracking circuits of the RKY, or the VIDIAN, which then generates an analog signal proportional to the motion of the black-white interface (Figure 3). The RKY is a device which records relative change in position of the border of the heart but does not provide absolute measurement of changes in position unless it is calibrated with an object of known size. The VIDIAN is a dual-window device capable of rapidly tracking with independent thresholds for either one or both sides of a moving object. The time lapse between the triggering of the two windows is proportional to the dimensions of the object delineated, thereby providing a continuous measurement of the extent of ventricular wall excursion. By recording the analog signal of wall motion on an oscillograph, the velocity of the ventricular wall excursion also can be determined.

As shown in Figure 4, the normal motion of the lateral external wall of the left ventricle recorded by the VIDIAN is characterized by: (1) an upright "a" wave (occurring 80-120 msec after the onset of the p wave on the apexcardiogram and coincident with the fourth heart sound as recorded by phonocardiography); (2) a second small positive deflection commencing simultaneously with the phase 1 component of the first heart sound (the rapid ascent ["C" point] of the apexcardiogram, and the initial rise of isovolumic pressure in the left ventricle following atrial contraction); (3) a downward deflection during ejection which begins with the initial upstroke of the high fidelity ascending aortic pressure pulse (coincident with the "E" point of the apexcardiogram) and ends after the notch on the ascending aortic pressure pulse; and (4) a diastolic phase marked by an initial steep ascent (corresponding with rapid filling wave of the apexcardiogram and ending with the third heart sound, as recorded on the phonocardiogram) and followed by a considerably more shallow ascent often punctuated by low frequency oscillations (Figure 4).

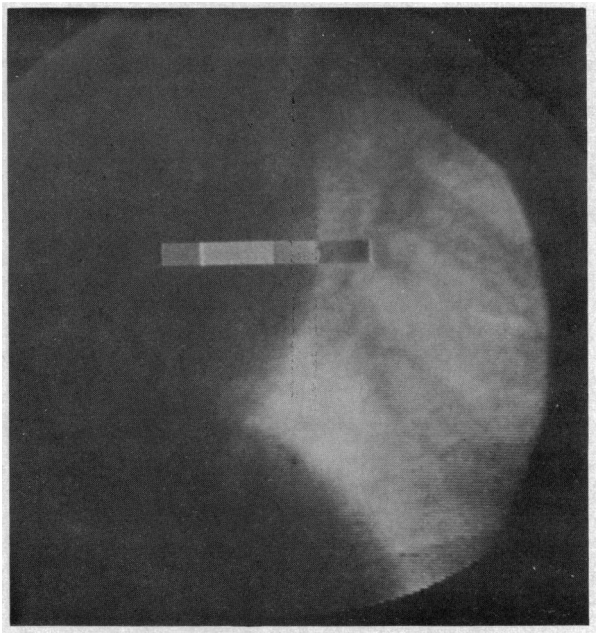

Figure 3.—Videodimension analyzer (VIDIAN) tracking fluoroscopic image of left heart border on television monitor. In practice the image is rotated so that long axis of left ventricle is perpendicular to raster lines of television. Left-hand window is stationary; right window is tracking the dynamic changes in position of left heart border.

Previous clinical studies of patients with acute myocardial infarction have determined that hypokinetic and dyskinetic areas of ventricular wall, some of which were not recognizable by the human eye, can be reliably detected with video-tracking (Figure 5). Moreover, wall motion abnormalities could not be visualized by fluoroscopy in 16 of 32 patients with chronic coronary artery disease in

*Manufactured by Biotronix, Silver Spring, Maryland.
†Manufactured by UCSD, Department of Bioengineering.

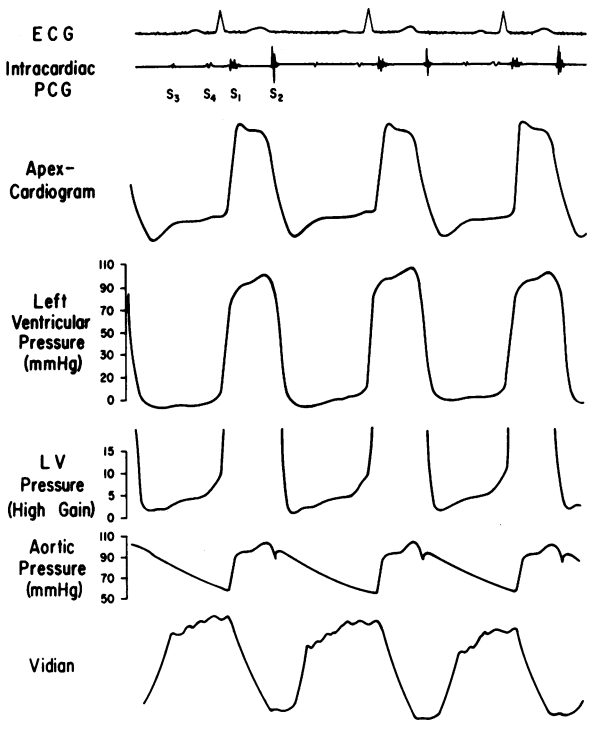

Figure 4.—Relative time sequence of electrocardiogram, intracardiac phonocardiogram, apexcardiogram, left ventricular pressure, ascending aortic pressure, and VIDIAN track of left ventricular wall (left anterior oblique projection). Note the rapid, slow, and atrial filling phases during diastole on the VIDIAN trace.

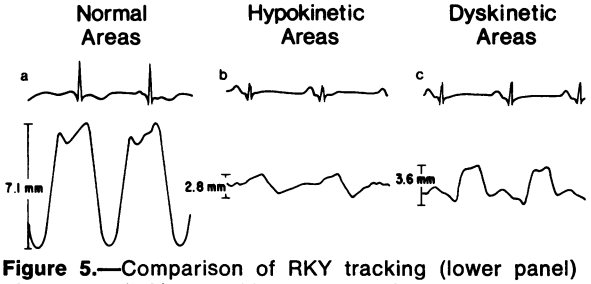

Figure 5.—Comparison of RKY tracking (lower panel) of normal (left), hypokinetic (center), and dyskinetic (right) areas of left ventricular wall. Electrocardiogram on top panel provided for timing of cardiac events.

whom such disorders could be detected by video-tracking. Areas of asynergy shown on left ventriculography in 18 patients were likewise reliably detected by radarkymography in 16 of the subjects.[22]

Recent observations on the response of the left ventricle to hand grip exercise (where heart rate and systemic arterial pressure increase) suggest that this intervention is useful for eliciting latent wall motion abnormalities or exaggerating pre-existent ones in patients with coronary heart disease.[23] Areas along the anterior and apical-lateral surface of the left ventricle are more readily detected than those along the inferior wall where the diaphragm inhibits clear delineation of the ventricular margins.

Video-tracking also has been used as a non-invasive means for the evaluation of the response of left ventricular wall motion to pharmacologic interventions, and we have recently studied the effects of beta-blockade on the characteristics of both normal and abnormal wall motion following intravenous administration of propranolol. It has been suggested that wall motion abnormalities may be worsened by propranolol. However, in areas which initially displayed dyskinetic or asynchronous outward movement, the amplitude and velocity of excursion were decreased by propranolol, resulting in a net diminution of the degree of outward bulging—that is, a net improvement in abnormal wall motion.[24] In areas of normal or hypokinetic wall motion, we found significant reductions in both the amplitude of the excursion and in the velocity of movement using the VIDIAN system.

A further use of video-tracking is in the study of diastolic filling patterns of the left ventricle. Comparisons of the shape and timing of the VIDIAN signal from the high lateral left ventricular wall margin in the left anterior oblique projection with ventricular volume measurements throughout the cardiac cycle have shown a striking similarity (Figure 6). Thus, a non-invasive determination of relative changes in ventricular dimensions by video tracking may prove to be a reliable method for recognizing those conditions with impeded ventricular filling—for example, constrictive pericarditis, mitral stenosis, or restrictive cardiomyopathy. When such diastolic filling curves are recorded with a simultaneously obtained diastolic left ventricular pressure, a beat-by-beat analysis of ventricular compliance and stiffness also is feasible (Figure 7). Assuming an exponential relationship, the slope of the plot of the natural logarithm of pressure versus the relative change in the left ventricular minor axis dimension, as measured by the VIDIAN, during the slow phase of ventricular filling, provides a coefficient of elasticity for the ventricle.

Video-tracking now provides an objective and quantitative non-invasive method for assessing the mechanical properties of the left ventricular wall during both systole and diastole. Abnormalities of

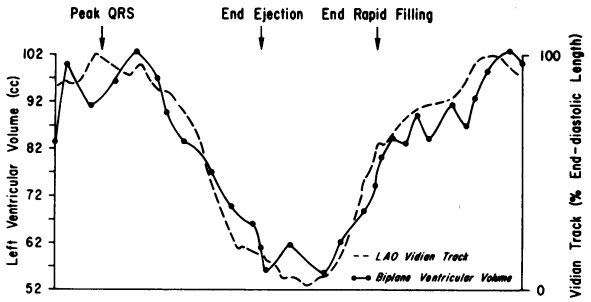

Figure 6.—Comparison of VIDIAN track of left heart border (dashed line) with measurement of left ventricular volume (solid line) throughout cardiac cycle.

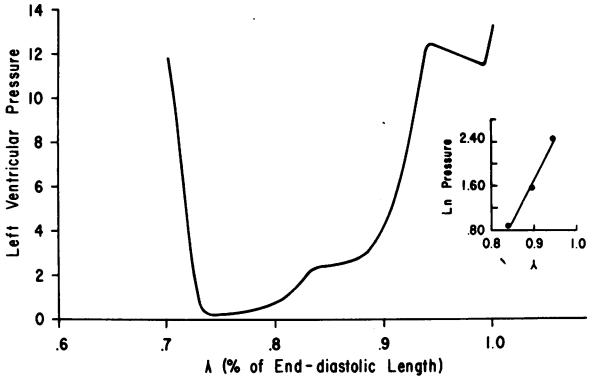

Figure 7.—High-fidelity left ventricular pressure (abscissa) plotted against percent of end-diastolic length (λ) (ordinate) throughout isovolumetric relaxation and diastole. Insert in right-hand corner depicts plot of natural logarithm of pressure versus λ during slow-filling phase of diastole. Rapid filling due to atrial contraction occurs between λ of 0.9 and 1.0.

the systolic contraction pattern appear to be more readily detected by video-tracking than by simple fluoroscopy alone and correlate reliably with findings on left ventriculography. Diastolic filling patterns, formerly assessed only by apexcardiography or tedious calculation of diastolic volumes from a cineventriculogram, can now be assessed by tracking the lateral left ventricular margin. The technique thus affords a new means of assessing ventricular function and filling, properties of particular importance to the understanding of cardiac performance in various forms of heart disease.

Dr. Ross: Another radiographic technique which employs only a plain, standardized chest roentgenogram recently was developed in our laboratory, and has now found considerable application in the serial follow-up of left ventricular size in cardiac patients and in the assessment of responses to pharmacologic interventions. Dr. Crawford has made several practical applications of this approach.

DR. MICHAEL CRAWFORD:* Left ventricular volume is an important factor in regulating cardiac performance, and the size of the left ventricle also has significant implications relative to the diagnosis and management of a variety of cardiovascular disorders. It would be useful, therefore, to have available a non-invasive method by which left ventricular size could be determined accurately and reproducibly. Plain radiographic techniques have the advantage of technical simplicity and widespread availability of equipment. The cardiothoracic ratio is commonly employed, although it has limitations because of its dependence upon thoracic configuration and because it does not specifically measure the left side of the heart.[25] Other plain radiographic techniques for calculating cardiac size and volume are more accurate,[26] but unlike the cardiothoracic ratio they require upright lateral films, prohibiting their application in acutely ill patients, and limiting their usefulness for assessing the heart under basal conditions. The need for an accurate technique for examining the left ventricle in such patients has led to the development of a standard technique for measuring the external left heart size.[27]

A frontal chest roentgenogram is taken with the patient in a horizontal position (or at a 45° angle, if necessary), small lead markers being taped to the chest at the sternal notch and xyphoid process. A small hand-held respirometer is used to insure a standard inspiratory volume of one liter above functional residual capacity, and the chest roentgenogram is triggered from the electrocardiogram to be exposed at end-diastole.[27] Subsequently, a vertical line is drawn on the film connecting the two lead markers, and a second, parallel vertical line is drawn tangential to the widest point of the left ventricular silhouette (Figure 8). The horizontal distance between these two lines, corrected for x-ray magnification and normalized per square meter of body surface area (m^2 BSA) represents the left heart dimension (LHD).

As with any plain radiographic technique, the LHD cannot be determined accurately in patients with a left pleural effusion, pericardial effusion, or pulmonary infiltrates that obscure the left heart border. This technique also may be unreliable in patients too dyspneic to hold their breath momentarily. Further, one must be careful that the patient does not perform a Valsalva maneuver, which

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is known to decrease heart size. Occasionally, pronounced elevation of the diaphragm or extreme enlargement of the right side of the heart may increase the LHD. With these precautions, the LHD has been found to be a reproducible and reliable measure of left ventricular size.[27]

One major use of the LHD measured in the basal, supine state is to determine whether or not left ventricular size is normal or abnormal in the individual patient. The LHD was found to correlate closely with left ventricular diameter (LVD) measured by cineangiographic techniques,[27] LVD being related to LHD by the regression equation LVD = 0.46 LHD + 23.5 mm ($r = 0.78$, $p < 0.001$). The average value for LHD in normal persons was found to be 44 ± 4 mm (1SD) per m^2 BSA and the upper limit of normal is considered to be 52 mm per m^2 BSA (+2 SD) (Figure 8). The LHD is routinely determined on admission to the Myocardial Infarction Research Unit at our institution and has been shown to be a valuable predictor of early and late survival after acute myocardial infarction. For example, early death occurred six times more frequently in those with an initially abnormal LHD ($p < .001$).[28]

Since the LHD is relatively unaffected by slight degrees of rotation of the patient, it has been a reliable technique for serial studies. During late follow-up after recovery from acute myocardial infarction, averaging ten months, patients with a persistently abnormal LHD had five times the death rate of those with a normal LHD. With one exception, all patients in New York Heart Association (NYHA) Class I-II had a normal LHD and the majority in NYHA Class III had an abnormal LHD.[28] Thus, the LHD has been a practicable method for serial studies and has proven useful for estimating survival and morbidity, as well as for effectively following the clinical course after an acute myocardial infarction.

In the cardiac catheterization laboratory a close correlation between the LHD and cineangiographic measurement of actual left ventricular diameter was shown to exist when changes in left ventricular volume were induced by acutely altering afterload, and other manipulations.[27] Therefore, another important application of the LHD has been to evaluate non-invasively the effects of various physiologic and pharmacologic interventions on the size of the left ventricle. For example, the normal response to submaximal isometric handgrip exercise is a small decrease in LHD.[29] In patients with a previous myocardial infarction NYHA Class I or II without major wall motion abnormalities, the LHD also decreased with handgrip, but in symptomatic patients (NYHA Class III) with major wall motion abnormalities the LHD usually increased. Thus, this measure provides a useful means of detecting an abnormal myocardial response to this physiologic stress.

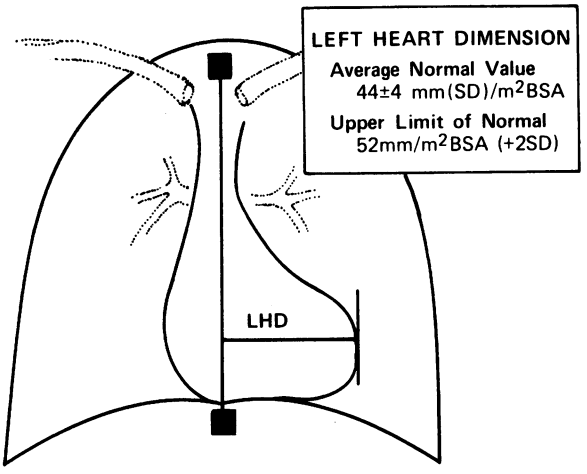

Figure 8.—Method for determining the external left heart dimension (LHD) from plain ECG triggered roentgenogram. The black squares indicate lead markers in the mid line between which a vertical line is drawn, the LHD representing the distance from the mid line to the widest point on the left heart border.

The LHD also has been used to assess the effects of pharmacologic interventions on ventricular size and performance. The administration of propranolol intravenously has been shown to cause an increase LHD in patients with coronary heart disease by a mean of 3 ± 7 (SD) mm ($p < .001$).[30] Preliminary results from our laboratory show that there is a small but significant increase in the LHD in patients with coronary heart disease who are taking oral propranolol as well. In some patients, this increase was reversed by adding a digitalis preparation. Figure 9 shows the values of LHD in a representative patient after two weeks of therapy with these drugs. The initial LHD was abnormal, and it was significantly increased further by propranolol therapy, an effect due at least in part to the observed slowing of heart rate; however, the addition of digoxin tended to reverse this increase. Thus, this approach can permit investigation of the effects of various pharmacologic agents on left ventricular size, as well as allow the selection of an optimal therapeutic program.

In conclusion, the left heart dimension has proved to be an accurate yet practical, non-in-

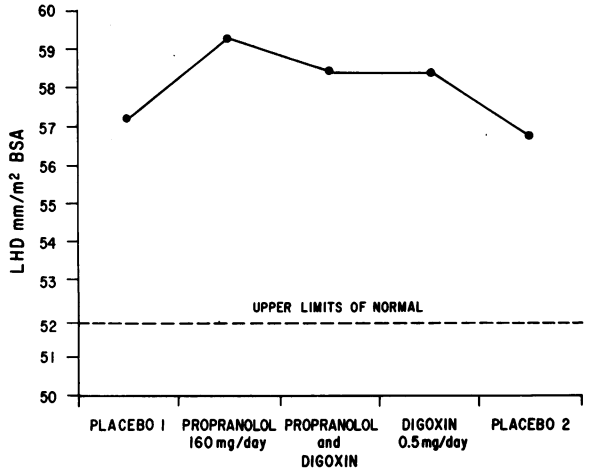

Figure 9.—Response of the left heart dimension (LHD) to two-week periods of oral drug therapy (each vertical line represents two weeks). The upper limits of normal (52 mm per M^2 BSA) for the left heart dimension is shown in this patient, who has marked left ventricular enlargement. The increase in left heart size induced by propranolol is partially reversed by digoxin therapy.

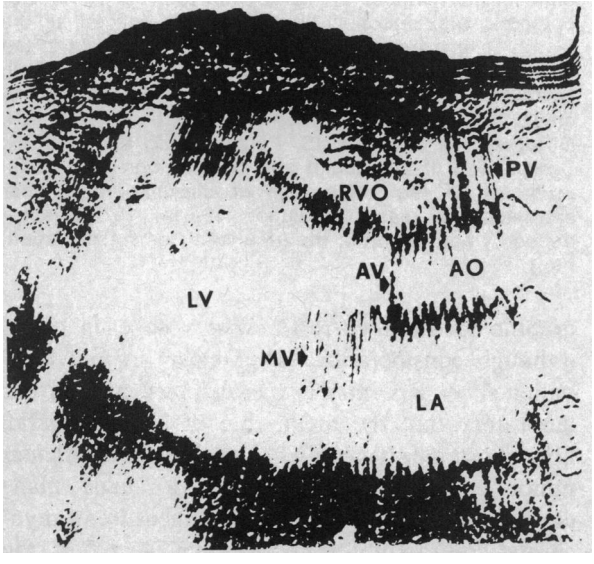

Figure 10.—Non-stop action B-scan made along the left fourth intercostal space in a patient with multichamber enlargement. The right-hand side of the picture shows the aortic root while the left side ends near the cardiac apex. LV = left ventricle, RVO = right ventricular outflow tract, LA = left atrium, MV = mitral valve leaflets, AV = aortic valve cusps, PV = pulmonic valve cusps.

vasive technique for assessing left ventricular size in the basal state. It can be easily performed on critically ill patients and is useful for day to day monitoring. An abnormal LHD after an acute myocardial infarction designates a higher risk group of patients who should perhaps be treated more vigorously. The method is useful as well for determining changes in left ventricular size after acute and chonic drug administration.

Dr. Ross: The newest and potentially perhaps most exciting method for cardiovascular exploration is ultrasound. This approach offers the opportunity of measuring absolute dimensions of cardiac structures as well as the dynamic motions of the cardiac chambers, valves, and great vessels. In addition, the recent development of multicrystal scanning ultrasound devices offers the promise of "dynamic pictures" of the heart, which eventually may rival in some ways those obtained by conventional cineangiography. Dr. Leopold will review certain recent advances in this field and discuss studies carried out in collaboration with Drs. Karliner and O'Rourke on the assessment of left ventricular performance in man by this technique.

DR. GEORGE LEOPOLD:* Single probe unidirectional echocardiography is now commonly employed in the non-invasive diagnosis of a variety of cardiovascular disorders, such as pericardial effusion,[31] mitral valve disease,[32,33] idiopathic hypertrophic subaortic stenosis,[34] left atrial myxoma,[35] and a wide range of congenital cardiac disorders. The conventional M-scan provides a time-motion display of various structures.

Another ultrasonic recording method which promises to yield significant information in the assessment of left ventricular anatomy and performance is the B-scan technique in which the ultrasound beam is swept along a single plane, the information being photographed from a storage oscilloscope. This method therefore provides a two-dimensional representation of the underlying cardiac anatomy rather than a time-motion plot. The plane most commonly chosen passes through the aortic root, mitral valve apparatus and body of the left ventricle (Figure 10). This is usually achieved by guiding the transducer along the third or fourth left intercostal space.

If desired, the returning echo information may be gaited to the electrocardiogram so that the heart is imaged only at a predetermined time in the cardiac cycle. The effects of cardiac motion are thereby negated. This technique has been termed "stop action" scanning.[36] A preliminary report by King[37] has indicated its usefulness in the estimation of left ventricular end systolic and end diastolic volumes. Alternatively, the recording may be made without gaiting (non-stop action) as pro-

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posed by Kikuchi.[38] With this technique the motion of all cardiac structures within the examination plane is recorded, yielding an image which is essentially an ultrasonic kymogram. Figure 10 shows such a scan along the long axis of the left ventricle of a patient with myocardopathy and dilatation of all cardiac chambers. The contours of the left ventricle, left atrium, and aortic root, as well as the positions of the mitral, aortic, and pulmonic cusps are easily appreciated. It is hoped that this technique will provide improved volumetric measurements of the individual chambers and possibly aid in detecting dyskinetic areas of the ventricular wall.

A recent innovation in instrumentation, as proposed by Bom,[39] is the use of a phased array of transducers so that all portions of the scan may be viewed simultaneously, rather than using a storage oscilloscope. A prototype model of such an instrument, currently being evaluated in our laboratory, employs twenty closely spaced crystals in a single transducer head, which as in conventional B-scanning, may be oriented along any desired cardiac plane. To date we have employed the long axis plane described above as well as a transverse plane placed in the second or third interspace to observe the spatial orientation of the great vessels to each other. Although early attempts at volumetric measurements have been disappointing because of difficulty in resolving precisely the endocardial echoes, the qualitative evaluation of cardiac anatomy afforded is impressive. Abnormalities such as chamber enlargement, overriding of the aorta, mitral-aortic discontinuity, and septal hypertrophy are easily detectable in this real-time type of imaging which may be thought of as ultrasonic fluoroscopy. It is hoped that further technical refinements of this instrument will increase even further the scope of its applicability.

Although cross-sectional techniques promise much for the future, most clinical work still is performed with single transducer, unidirectional equipment. Assessment of left ventricular function is an important clinical application of this technique. However, as with other non-invasive methods, careful validation of the accuracy of this type of echocardiography by comparison with conventional hemodynamic-angiographic methods is essential. Ideally, such comparative studies should be carried out in the same patients.

Several studies have indicated that the ejection fraction (ratio of stroke volume to end-diastolic volume) determined by ultrasonic and cineangiographic methods correlate well with each other, although considerable scatter exists in individual patients.[40,41] Recently it was demonstrated in our laboratory that the mean rate of circumferential fiber shortening (mean Vcf) at the left ventricular minor equator, determined on a single plane cineangiogram, provides a useful measure of myocardial contractility.[42] To calculate mean Vcf, the extent of internal myocardial wall shortening from end diastole to end systole is divided by the ejection time; the value thus obtained then is corrected for end-diastolic circumference and the result expressed in circumferences per second (circ/sec). Normalization in this fashion permits comparison among patients. Since this angiographic measurement is derived from a chord drawn perpendicular to the long axis of the left ventricle, placement of an ultrasound beam in a similar plane should yield comparable results for mean wall shortening velocity (Figure 11). Indeed, reports of mean Vcf by echo have appeared with average normal values ranging from 0.92 to 1.45 circ/sec,[43,44] while mean

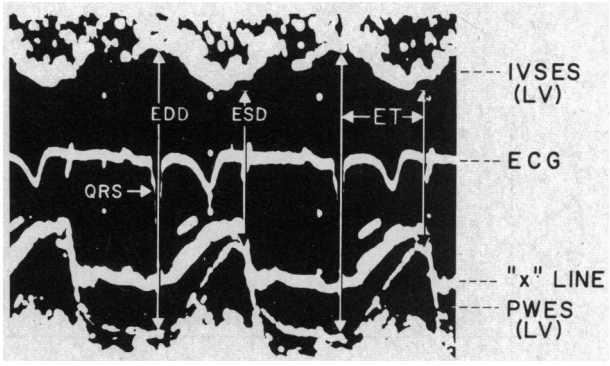

Figure 11.—Echocardiogram which shows the endocardial surface of the intraventricular septum (IVSES) and left ventricular posterior wall (PWES) as well as the "x" line. Although its exact identity has not been established, the "x" line is thought to represent echoes reflected from the mitral valve apparatus. Automatically incorporated into the display are the simultaneous electrocardiogram and time-distance markers. Distance is plotted on the vertical axis and time on the horizontal. End-diastolic dimension (EDD) between endocardial surfaces was measured along a vertical line drawn through the QRS complex. The systolic dimension (ESD) was defined as the smallest distance separating the endocardial surfaces of the septum and left ventricular posterior wall. Ejection time (ET) was defined as the length of time from the peak of the QRS complex to the maximum excursion of the left ventricular posterior wall, less 50 msec for the pre-ejection period when no appreciable fiber shortening takes place. (From Cooper RH, O'Rourke RA, Karliner JS, Peterson KL, Leopold GR: Comparison of ultrasound and cineangiographic measurements of the mean rate of circumferential fiber shortening in man. Circulation 46:914, 1972. Reproduced by permission of the American Heart Association, Inc.)

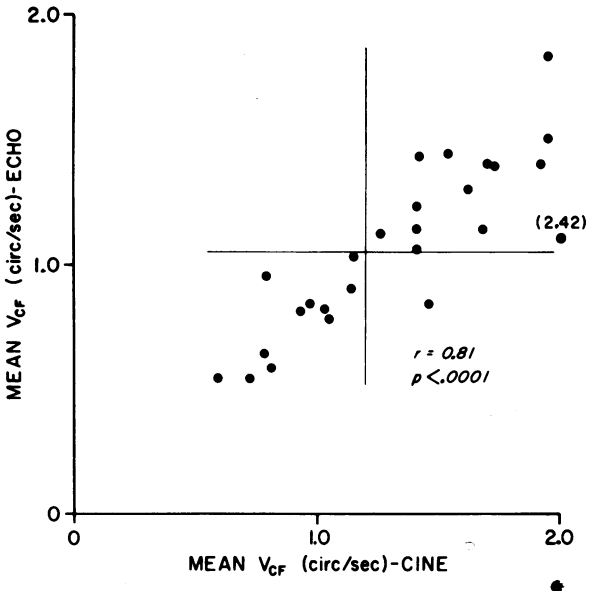

Figure 12.—Mean Vcf by ultrasound is plotted against mean Vcf determined by cineangiography. The crossed lines represent the lower limits of normal for each measurement (1.05 circ per sec for mean Vcf by echo and 1.20 circ per sec for mean Vcf by ciné). (From Cooper RH, O'Rourke RA, Karliner JS, Peterson KL, Leopold GR: Comparison of ultrasound and cineangiographic measurements of mean rate of circumferential fiber shortening in man. Circulation 46:914, 1972. Reproduced by permission of the American Heart Association, Inc.)

Vcf by ciné in the normal subject averages 1.50 circ/sec, with a lower limit of 1.2 circ/sec.[42]

Because of the wide range of mean Vcf by echo reported by others, we sought to compare echo and ciné measurements of mean Vcf in the same patients.[45] In 15 patients considered to have normal left ventricular function, the average mean Vcf determined by ultrasound was 1.29 ± 0.23 (1 SD) circ/sec, while in 13 patients with reduced left ventricular performance this value was 0.75 ± 0.16 circ/sec. The difference between these two values was highly significant. Values obtained by the echo technique showed a high degree of correlation with the results obtained by cineangiography and separated normal from abnormal left ventricular function in 27 of the 28 patients (Figure 12). The range of normal values was similar to that reported by McDonald and co-workers,[46] smaller than the normal range reported by Paraskos and associates,[44] and larger than that noted by Fortuin, Hood and Craige.[43] Reasons for the discrepancies among the various studies include differences in the plane of the left ventricle examined, alternative methods of normalization, and use of epicardial rather than endocardial surfaces of the posterior left ventricular wall. Since epicardial surface excursion is less than endocardial movement, owing to thickening of the left ventricular wall during systole, calculations using the former are subject to considerable error, the results being an underestimation of mean shortening velocity.

Whether or not internal shortening velocity measured in one plane in patients with wall motion abnormalities due to coronary artery disease can accurately characterize left ventricular function has been open to question. Accordingly, we recently examined the relation between mean Vcf determined by both the ciné and ultrasound techniques in 21 patients with abnormal wall motion.[47] The results indicated that the ultrasound technique was accurate in separating normal from impaired left ventricular function in all of the patients studied. Echo and ciné determinations of end-diastolic volume also showed a high degree of correlation in patients with wall motion abnormalities, although considerable volume overestimation by echo was observed in patients with widespread anterior akinesis or marked left ventricular enlargement.

Mean posterior wall velocity, especially at the left ventricular epicardial surface, is simple to measure by ultrasound. Further, it has been suggested that posterior wall velocity is sensitive to physiologic and pharmacologic interventions,[48] and it has been proposed as a measure of the inotropic state of the left ventricle.[49] In nine normal persons and in 39 patients with angiographically documented coronary artery disease, we compared mean endocardial posterior wall velocity by echo with ultrasound and cineangiographic calculations of ejection fraction and mean Vcf. In these patients we were unable to demonstrate a good correlation between mean posterior wall velocity, whether determined at the epicardial or endocardial surfaces, and mean Vcf and ejection fraction determined by cineangiography.[50] Moreover, of 25 patients with a reduced mean Vcf by echo, as described above, only three had a depressed mean endocardial posterior wall velocity. In comparison with other measures of myocardial performance, estimation of mean posterior wall velocity generally tended to overestimate left ventricular function. This finding may result from the absence of abnormal posterior wall movement in many patients with coronary artery disease as well as from the anterior motion of the whole heart during systole, which increases the recorded anterior movement of the posterior left ventricular wall.[46] Further,

large day-to-day variations occurred in posterior wall velocity measured at the epicardial surface both in normal persons and patients with acute myocardial infarction. These observations indicate that ultrasonic measurement of mean posterior wall velocity provides an unreliable index of left ventricular performance.

Dr. Ross: These studies are illustrative, I think, of the progress being made in this rapidly developing field. As ultrasound methods gain increasing precision and are validated by direct comparison with established methods, we may look for increasing reliance on diagnostic ultrasound in the assessment of cardiac anatomy and function.

The final approach that we shall consider is the use of injected radioisotopes. The development of Anger type cameras has now allowed adequate visualization of the cardiac chambers and great vessels, and recently efforts have been made to apply this technique to the assessment of left ventricular function, and to study the myocardium in patients with coronary heart disease. We shall turn next to consideration of the use of ventricular imaging in the assessment of cardiac function. Drs. Karliner and Sobel have been interested in particular in the application of these methods in patients with acute myocardial infarction.

Radioisotope Angiocardiography

DR. JOEL S. KARLINER* AND DR. BURTON E. SOBEL:† Conventional cineangiographic methods for visualization of the chambers of the heart and the great vessels are of unequivocal value in patients with chronic cardiovascular disease and in defining the cause of certain acute disorders. However, they require cardiac catheterization and the rapid injection of radiopaque contrast medium under high pressure. These procedures are not without hazard, particularly in patients acutely ill with electrical or functional instability of the myocardium. Furthermore, although serial studies with contrast media are possible, frequent repeated cardiac catheterizations are potentially hazardous and are associated with some discomfort. Accordingly, considerable effort has been applied to development of other means, such as radionuclide angiocardiography, by which the cardiac chambers can be visualized. This procedure can be performed by peripheral venous injection of radionuclides and subsequent detection of the material with a gamma camera. It entails no significant risk, is virtually free from morbidity, and produces no hemodynamic perturbations.

Ventricular volumes can be quantified readily by radioisotope angiocardiography in experimental animals[51] and it has been shown that the method is applicable for cardiac visualization in patients with chronic cardiovascular disease.[52] Accordingly, we extended the technique to patients with acute myocardial infarction in a recent investigation designed to determine whether accurate assessment of left ventricular performance was possible in critically ill patients and to ascertain whether serial studies would provide useful information in such patients, thereby obviating the need for procedures utilizing contrast media.[53]

Radionuclide angiocardiography is performed by injecting a bolus of 7 to 15 mC of technetium-99m (sodium pertechnetate) through a Swan-Ganz catheter which has been floated into the pulmonary artery, or through an inlying peripheral venous catheter. Resolution is somewhat better when pulmonary arterial injection is utilized; however, acceptable results can be obtained by peripheral venous injection. The radiation exposure (0.06 to 0.16 rads per dose) is in the range of a conventional diagnostic x-ray and the radionuclide has a physical half-life of only six hours. An Anger-type scintillation camera is used for imaging the pattern of flow through the heart chambers. Sequentially obtained images are recorded and stored on magnetic tape along with the simultaneously recorded electrocardiogram. Both the stored video signal and the electrocardiogram are then replayed. With the use of a gating discriminator triggered by the electrocardiogram, images at either end-diastole or end-systole are summed and displayed on a storage oscilloscope. The cardiac silhouettes at each of these selected times are photographed directly, projected on a screen, and traced (Figure 13). Areas are determined by planimetry with appropriate corrections for magnification. These data provide information sufficient to calculate left ventricular end-diastolic volume, stroke volume (end-diastolic volume minus end-systolic volume), and ejection fraction (the ratio of stroke volume to end-diastolic volume).[53]

In 64 patients with acute myocardial infarction studied in the Myocardial Infarction Research Unit, left ventricular end-diastolic volumes determined by this technique averaged 101 ± 7 (1 SEM) ml/M^2, and it was elevated (>90 ml/M^2) in 47 patients. Initial ejection fraction

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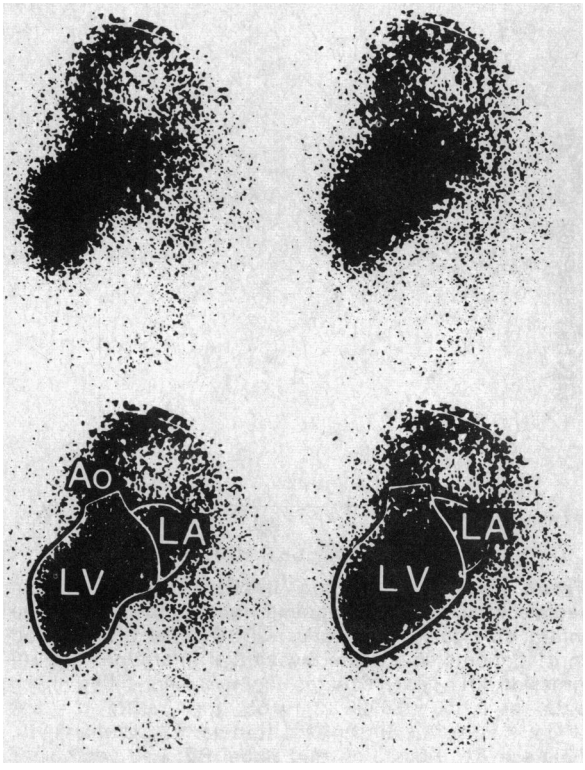

Figure 13.—End-systolic (left panel) and end-diastolic (right panel) images in the lateral projection obtained after peripheral venous injection of technetrium-99m in a patient with acute myocardial infarction. Anterior wall akinesis is apparent. In the bottom panels the silhouettes are outlined in order to depict the planimetered area used for volume and ejection fraction calculations. Papillary muscle images were not excluded from the planimetered areas. Since Sandler and Dodge have demonstrated that the radii in the postero-anterior and lateral projections are virtually identical, the formula for single frontal plane volume calculations proposed by these investigators has been applied to volume calculations in the lateral (L) projection: $V_L = 4/3\pi \times [D_L/2]^2 \times L_L/2$; $D_L/2$ = chamber radius in the lateral projection and L_L = the longest measured length in the lateral projection. The lateral chamber radius is derived from $D_L/2 = 2A/\pi\ L_L$; A = the planimetered area of the lateral left ventricular image. AO = aorta; LA = left atrium. (From Kostuk WJ, Ehsani AA, Karliner JS, Ashburn WL, Peterson KL, Ross J Jr., and Sobel BE: Left ventricular performance after myocardial infarction assessed by radioisotope angiocardiography. Circulation 47:244, 1973. Reproduced by permission of the American Heart Association, Inc.)

averaged $0.38 \pm .03$ and was reduced (<0.52) in 58 (90 percent) of the patients. The extent of shortening of the diameter at the minor left ventricular equator determined from radionuclide angiocardiograms was decreased in 51 patients, and the reduction in fiber shortening was not consistently related to the site of infarction determined electrocardiographically. In 53 patients who subsequently recovered from the acute infarction, the

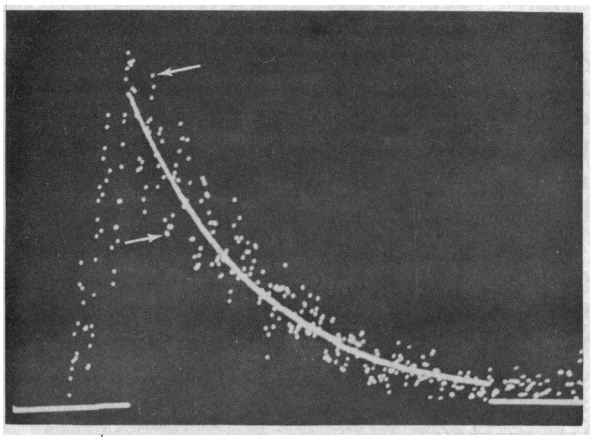

Figure 14.—Computer plot of time (abscissa) and counts (ordinate) during passage through the left ventricle of a radioactive bolus injected into the pulmonary artery. Each point represents total counts from "flagged" region corresponding to the left ventricle (corrected for background) for 0.04 sec. Cyclical change in counts is due to the beat-by-beat ejection of the tracer from the chamber. From the high and low values (arrows) per cardiac cycle, ejection fraction can be calculated. From the derived slope of the curve (heavy line) end-diastolic volume can be estimated.

initial ejection fraction averaged 0.40 ± 0.02, compared with 0.26 ± 0.07 ($p<0.05$) in 11 patients who died within one month.

Radionuclide angiocardiograms are useful in this setting also for detection of left ventricular wall motion disorders and mitral regurgitation. Forty-seven of the 64 patients with acute infarction exhibited abnormal wall motion detectable by the radionuclide technique and confirmed by radarkymography. Serial radionuclide angiocardiograms (obtained six hours to one month after onset of infarction) showed improvement of ventricular function in 30 of 55 patients. Left ventricular function assessed by this technique was unchanged in serial studies in 12 patients. Deterioration was apparent in 13 patients.

Additional quantitative methods for estimating left ventricular volume and ejection fraction are being investigated in a number of laboratories as well as our own.[54-56] Regions corresponding to the entire left ventricle are electronically "flagged" for computer evaluation, and a histogram of counts plotted against time is displayed for analysis (Figure 14). After correction for background contributions, the cyclical high (diastole) and low (systole) count values (Figure 14, arrows), which result from the beat-by-beat ejection of the labeled material from the left ventricle, are used to calculate ejection fraction (peak-to-valley/peak-to-zero level).

Dr. Ross: One of the most difficult areas of clinical investigation concerns the evaluation of acutely ill patients such as those with acute myocardial infarction. Dr. Sobel, could you expand a bit further on the application of this non-invasive measure of left ventricular function as it correlates with the size of an acute myocardial infarction?

Dr. Sobel: It is likely that a major determinant of impairment of ventricular performance after myocardial infarction is infarct size.[50] Accordingly, we compared infarct size estimated from analysis of serial serum CPK changes to ejection fraction determined by radionuclide angiocardiography in the same patients.

We have utilized a biochemical index to assess the extent of ischemic injury to the myocardium ("infarct size") in patients with acute myocardial infarction. This approach depends on mathematical analysis of serial changes in serum creatine phosphokinase (CPK) activity.[57] Since the amount of CPK released from the heart is related to the extent of ischemic injury, serial serum changes are used to estimate CPK released as a function of time. The analysis is based on the concept that changes in serum CPK activity reflect two competing phenomena: (1) release of CPK from myocardium undergoing necrosis, and (2) clearance of enzyme activity from blood, by mechanisms not yet thoroughly elucidated. When this technique was used to assess infarct size in patients we found that prognosis after myocardial infarction was closely related to estimated infarct size.[58]

The calculated infarct size in a group of patients with acute myocardial infarction is plotted against their ejection fractions, estimated by radionuclide angiography, in Figure 15. The data indicate that, in general, the severity of impairment of left ventricular function, reflected by the decrease in ejection fraction, was linearly related to infarct size. Scatter in the data is of course not surprising since ejection fraction is influenced also by numerous factors affecting preload and afterload.[53]

Thus, our experience with both of these non-invasive techniques in acutely ill patients indicates that radionuclide angiocardiography is extremely helpful in the assessment of left ventricular performance without injection of potentially hazardous contrast media in critically ill patients and that meaningful estimates of infarct size can be obtained readily by analysis of serial changes in serum CPK activity. Furthermore, it is becoming increasingly clear that infarct size is a major determinant of the severity of impairment of left ventricular function during the acute phase, and of prognosis in patients recovering from acute myocardial infarction.

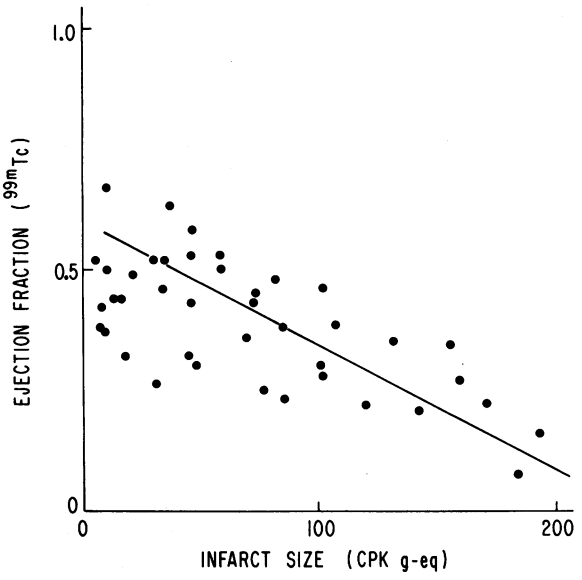

Figure 15.—Initial ejection fraction calculated from radioisotope angiocardiograms compared to estimated infarct size determined by the UCSD serial CPK method in 41 patients with acute myocardial infarction. The regression line (least squares method) best fitting these data is: $Y = -0.0032 \times +0.58$, $r = -0.73$, $n = 41$. (From Kostuk WJ, Ehsani AA, Karliner JS, Ashburn WL, Peterson KS, Ross J Jr, and Sobel BE: Left ventricular performance after myocardial infarction assessed by radioisotope angiocardiography. Circulation 47:247, 1973. Reproduced by permission of the American Heart Association, Inc.)

Intravenous Radioisotopes for Myocardial Imaging

Dr. Ross: Our final presentation concerns the use of a non-invasive technique for myocardial imaging which employs intravenously administered radioisotopes. Dr. William Ashburn will describe the current state of this new technique, which potentially is of great practical importance in the assessment of patients with coronary heart disease and acute myocardial infarction.

DR. WILLIAM L. ASHBURN:* Ever since the observations by Carr and others[60-66] that certain intravenously administered radioactive substances such as cesium, potassium and rubidium concentrate in normal but not in infarcted myocardium in sufficient amounts to permit external imaging, investigators have continued to search for ways to pictorially demonstrate the extent and location of

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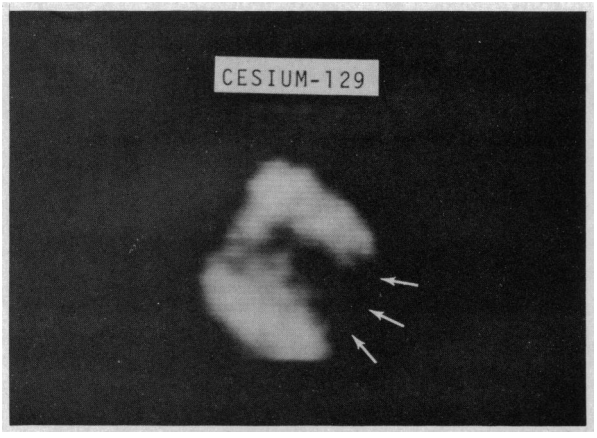

Figure 16.—Anterior ^{129}Cs myocardial image demonstrating "cold" deflect (arrows) in the area of known myocardial infarction in a 53-year-old man.

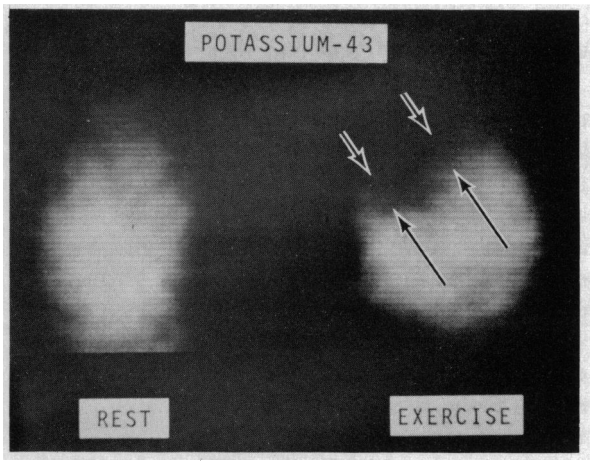

Figure 17.—Anterior ^{43}K myocardial images obtained at rest and exercise (see text). Large region of transient ischemia is suggested (arrows) on the study which followed a period of angina induced by treadmill exercise. Note also the increase in heart size with exercise.

non-perfused myocardium by non-invasive radioisotope scanning using intravenous injections.

At present, the two most commonly employed radioactive agents for myocardial imaging are ^{129}Cs (32 hr. half-life) and ^{43}K (22 hr. half-life). Both of these radioisotopes are cyclotron-produced in limited quantities, although ^{43}K can be produced in large nuclear reactors. These radioisotopes emit gamma rays having approximately the same energy as ^{131}I (350-400 kev range), although ^{43}K also emits several higher energy photons the effects of which place special requirements on shielding and collimator design. Even so, useful images of myocardial uptake can be obtained with both rectilinear scanners and scintillation cameras.

Following the intravenous administration of ^{129}Cs, the maximum myocardial concentration of the tracer occurs at about 1 hour, at which time approximately 5 percent of the injected dose is present within the heart muscle. Identification of the heart outline is complicated by the concentration of ^{129}Cs in adjacent organs such as the liver, stomach, diaphragm and other soft tissues. However, some of the best images of infarcted myocardium, which appear as "cold" defects have been obtained with this radioactive agent (Figure 16). Because the rate of tracer clearance from normal myocardium is relatively slow, ample time for multiple view imaging is afforded.

By contrast, ^{43}K reaches maximum myocardial concentration within about 5 minutes following intravenous administration. The rate of clearance is relatively rapid with an effective half-time of approximately three to four hours in normal persons. Background radiation from adjacent soft tissues is somewhat less than with ^{129}Cs, but because of the higher energy photon contributions, some compromises in image resolution are necessary.

Although ischemia, infarction and scarring each may be associated with clearly outlined areas of reduced myocardial concentration of the radioisotopes, these cannot ordinarily be distinguished by the appearance of the myocardial image. However, Zaret and coworkers[67] have taken advantage of the fact that ^{43}K is rapidly accumulated by normal but not by ischemic myocardium and have performed the imaging procedure immediately following a period of treadmill exercise stress to the point of angina or ST-wave changes, in order to maximally intensify the difference between normal and acutely ischemic tissue. A repeat study is then made on the following day while the patient is at rest and compared with the "exercise" image to note any apparent changes which suggest transiently ischemic regions of myocardium (Figure 17).

Since these procedures are non-invasive, considerable interest has arisen in attempting to apply such examinations in the evaluation of patients with coronary artery disease with or without previous myocardial infarction. So far, there has not been sufficient clinical experience with these techniques to determine their ultimate role in the diagnostic evaluation of patients being considered for revascularization surgery. Myocardial imaging is also being applied on an investigational basis in patients with acute myocardial infarction in order to determine whether the apparent size and location of the "cold defect" or any changing pattern

during the early stages of the disease may aid in clinical prognostication and therapy.

Other radioactive substances have been mentioned as possible myocardial imaging agents and are being evaluated, by and large, in those laboratories having access to cyclotron produced radioisotopes. At present, ^{13}N (10 min. half life) labeled ammonia as well as other cyclotron produced radionuclides are being evaluated by Harper and coworkers[68] at the University of Chicago as well as by other workers. Thallium-203 is also being evaluated by this group, as well as by Lebowitz et al[69] at the Brookhaven National Laboratory. A variety of compounds labeled with ^{11}C and ^{125}I are being investigated by Poe and Eber[70] at UCLA as well as at a few other centers having cyclotrons. In addition, Bonte et al[71] at the University of Texas in Dallas have made a preliminary report concerning the use of oleic acid labeled with appropriate radioisotopes as potentially useful myocardial imaging agents.

Still another approach in myocardial imaging is receiving increasing attention. Since the original observations by Gorton et al[72] and Malek et al[73] that certain compounds appear to concentrate in infarcted myocardial tissue in sufficient quantities for external imaging, other workers have begun to search for suitable radioactive agents which might permit specific labeling of myocardial infarcts. In this category, ^{67}Ga citrate is being investigated by Johnston and coworkers[74] at the Clinical Center, National Institutes of Health, and ^{99}Tc-labeled tetracycline is undergoing evaluation by Holman and coworkers[75] in Boston. Another potentially useful compound appears to be ^{197}Hg labeled cysteinide.[76]

The results of these investigations indicate that it may become possible to satisfactorily image viable and/or infarcted myocardium as certain improvements in instrumentation and data handling techniques become available. It may be realistic to expect that we will be able in the not too distant future to distinguish between regions of healthy and under-perfused myocardium by non-invasive radioisotope imaging techniques.

Dr. Ross: In concluding this specialty conference, I should like to emphasize that some of the techniques described are still in the investigative stage, whereas others appear capable of providing clinically useful information about cardiac function at their current state of development. Within the latter category we may include the systolic time intervals, the plain radiographic and video methods, left ventricular imaging by radioisotopes, and standard diagnostic ultrasound. However, the potential for further improvements in the usefulness of each of these techniques as quantitative tools seems great, particularly exciting being the advances in ultrasonic methods. Rapid developments in radioisotope technology also offer the promise of better cardiac visualization, the ability to perform dynamic washout studies, as well as the possibility of detection of myocardial perfusion defects. It is not unreasonable to hope, therefore, that in the relatively near future it will become possible to reliably assess the cardiac patient by applying a combination of these indirect methods and thereby obviate the need for cardiac catheterization and angiography in many subjects.

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